

Predictive Models of Emphysema Progression in HIV

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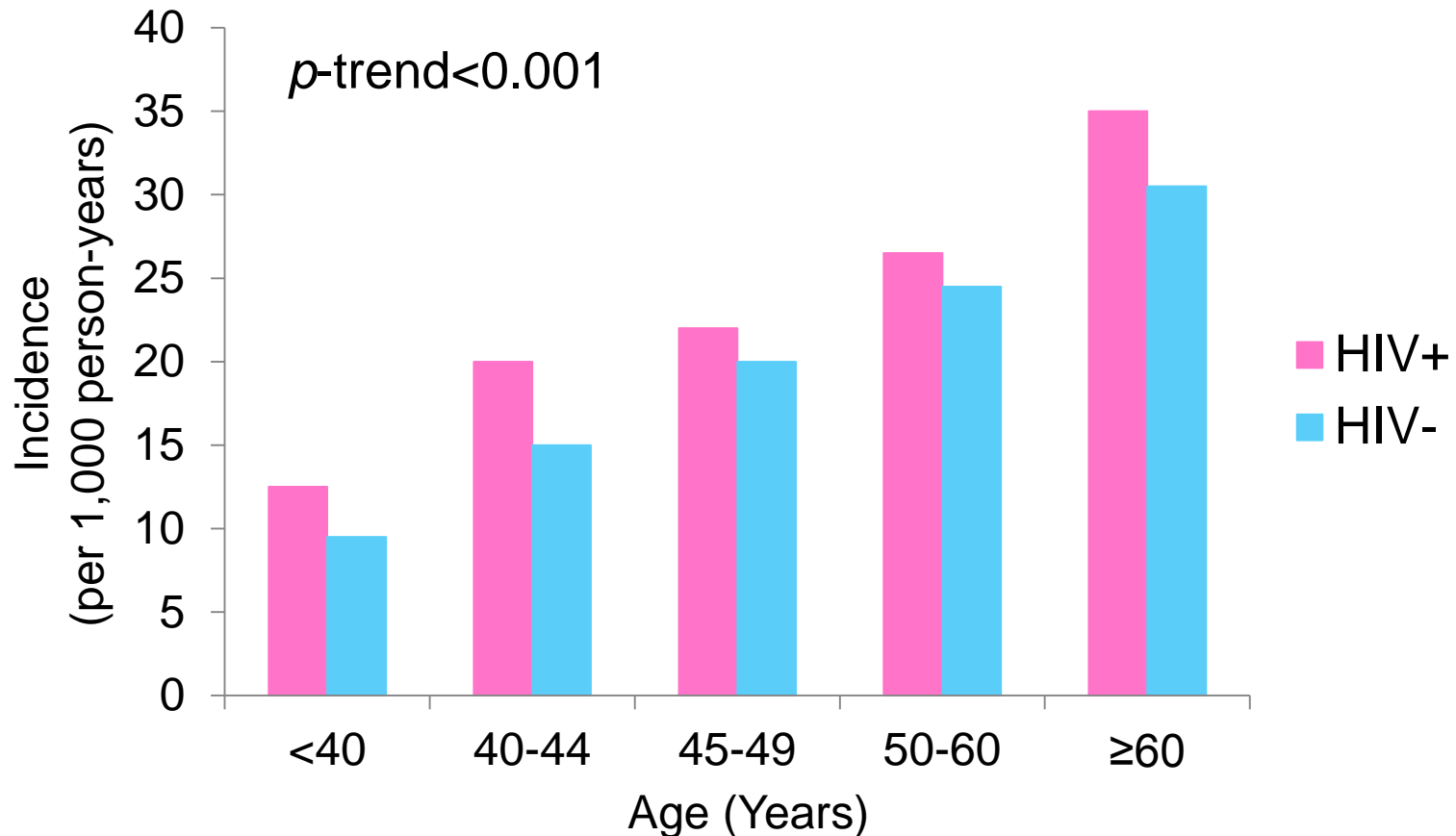
Centre for
Heart Lung Innovation
UBC and St. Paul's Hospital



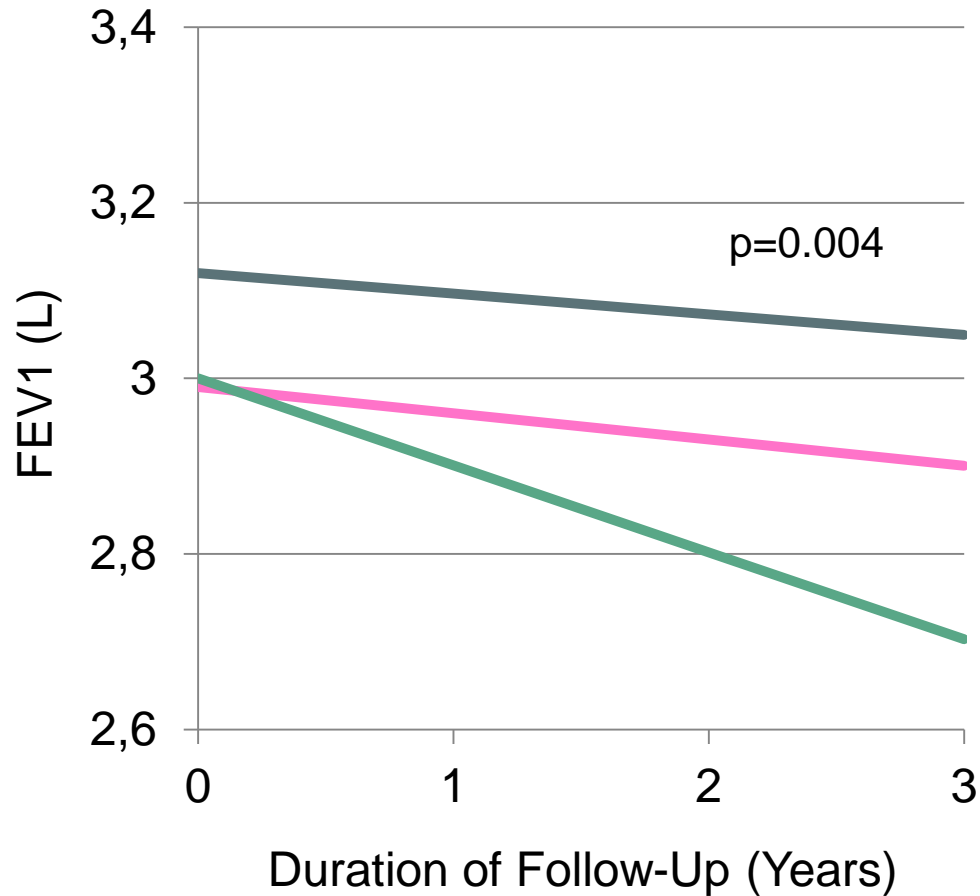
a place of mind

COPD: An Emerging Comorbidity

- Incidence rates of COPD appear to be higher in HIV compared to non-HIV patients

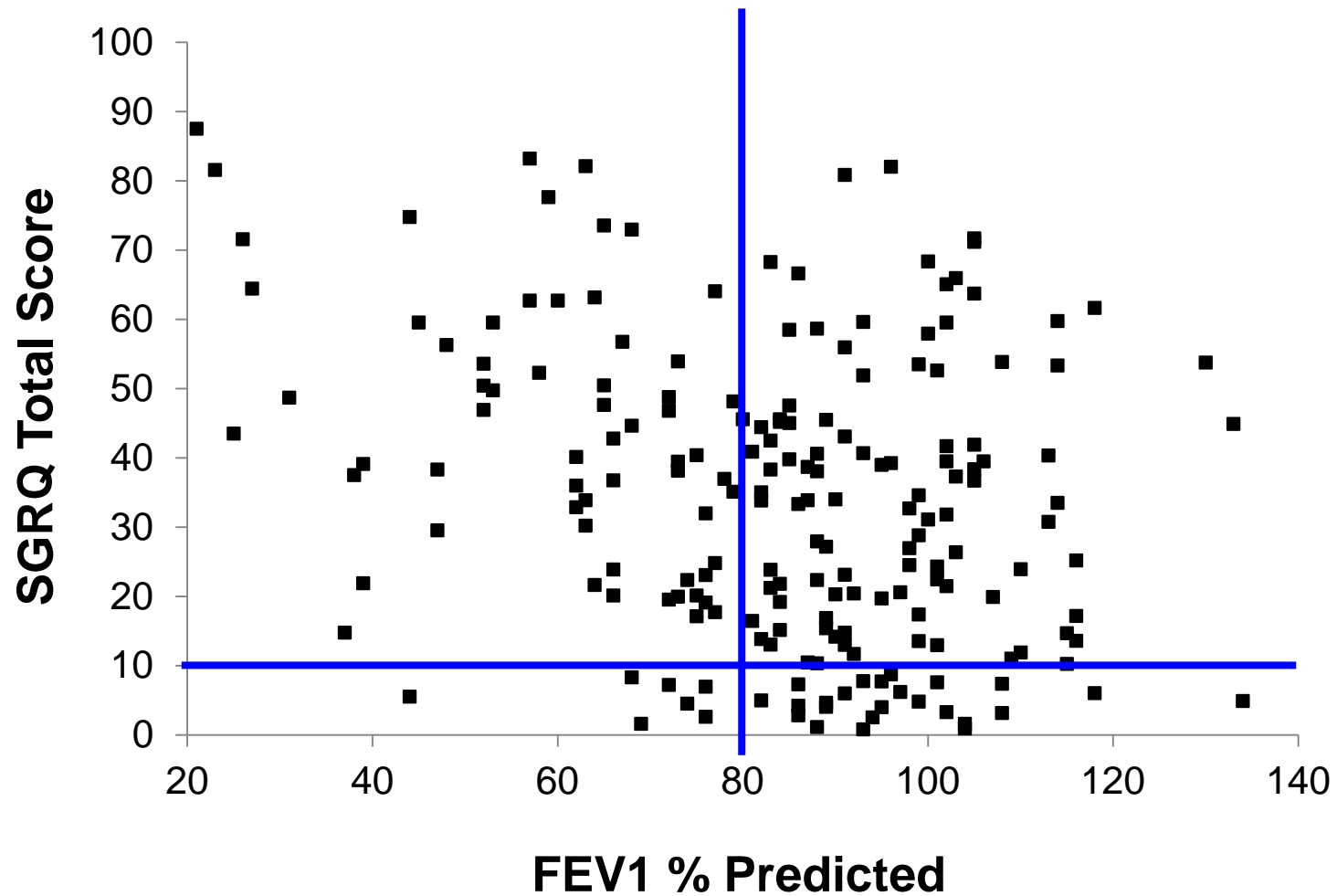


Faster Lung Function Decline

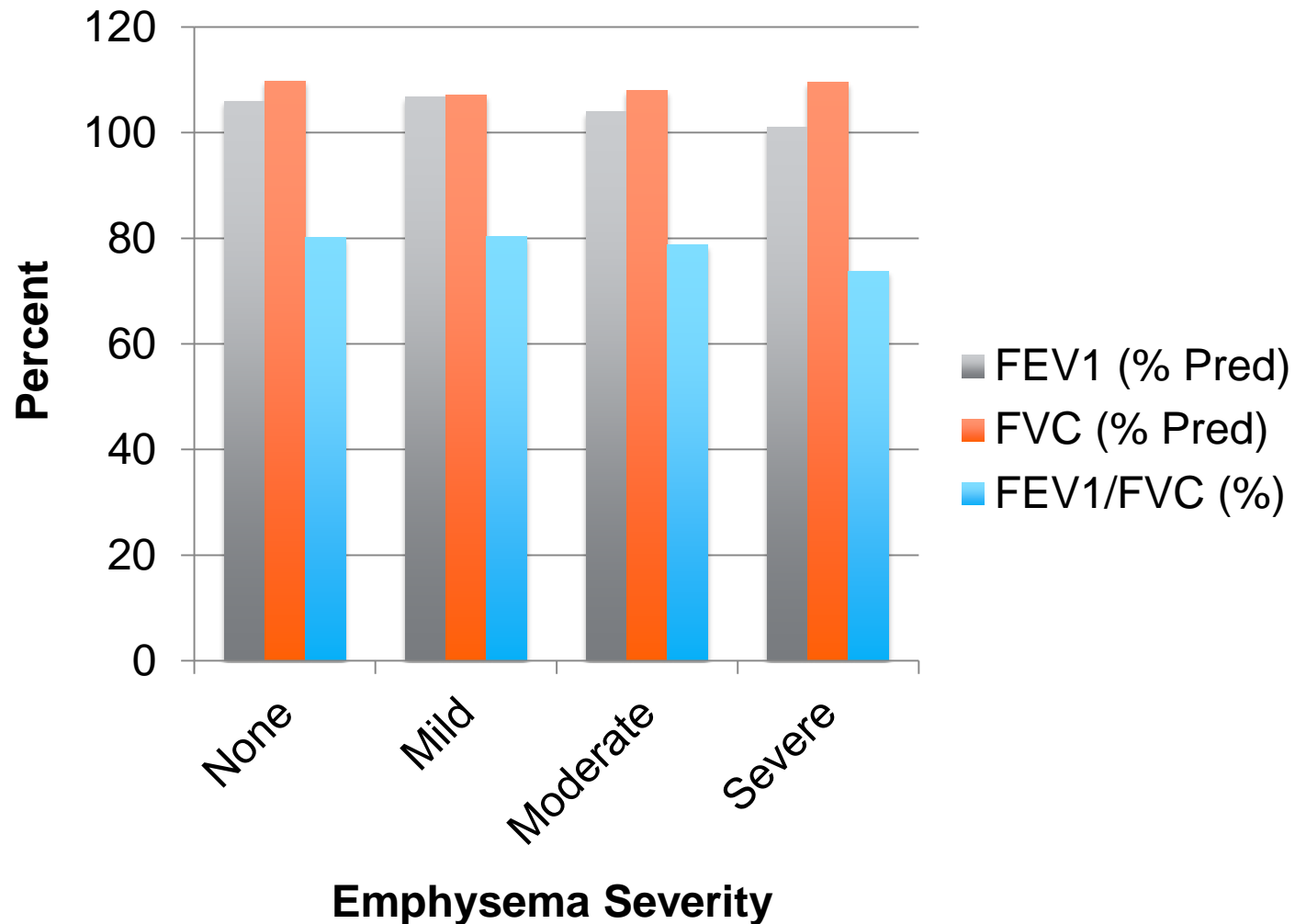


- HIV-
- HIV+/VL<70,000 copies/mL
- HIV+/VL>70,000 copies/mL

Worse Respiratory Symptoms



The Emphysema Phenotype in HIV



Clinical Significance of Emphysema

- >25% emphysema is significantly associated with a higher MRC dyspnea score, worse 6 minute walk distance, and higher BODE index in COPD¹
- Emphysema is also significantly associated with worse St. George's Respiratory Questionnaire scores²

¹Diaz AA. Chest 2010.

²Gietema HA. Respir Med 2013.

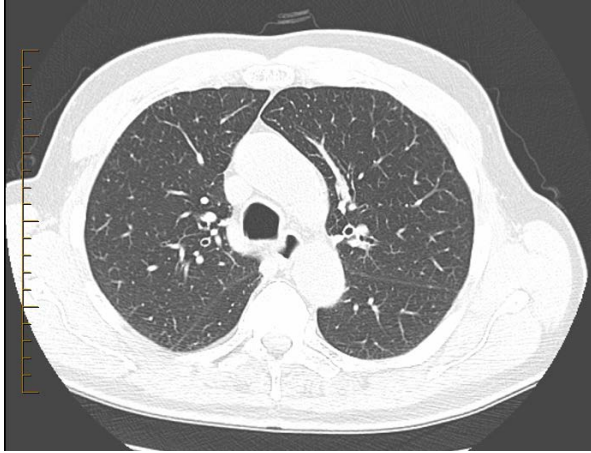
Study Objective

To determine the predictors of emphysema progression over a five year period in HIV and compare the prevalence of progression to a non-HIV population

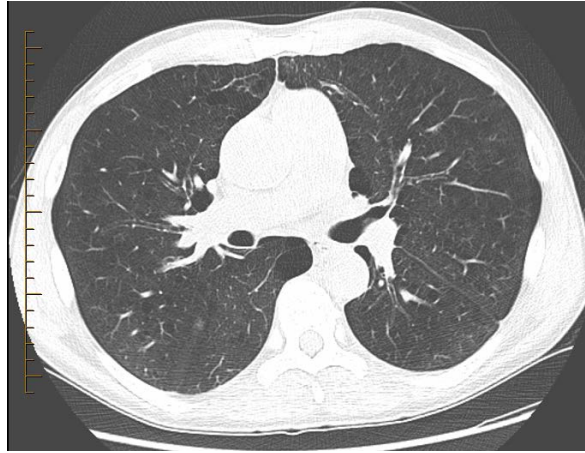
Methods

- **HIV Study Population**
 - 345 HIV+ patients with ≥ 2 chest CT scans
 - Enrolled in an HIV Metabolic Clinic in Modena, Italy
 - Median Time Span (IQR) Between First and Last CT scans
= 3.36 years (2.07, 4.99)

Qualitative Emphysema Scoring



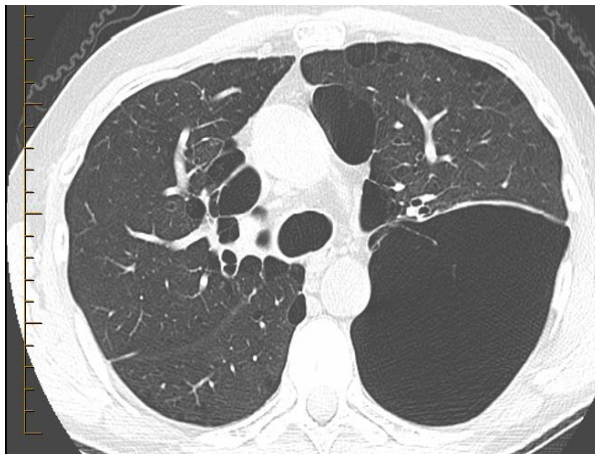
0



1=1-25%



2=26-50%

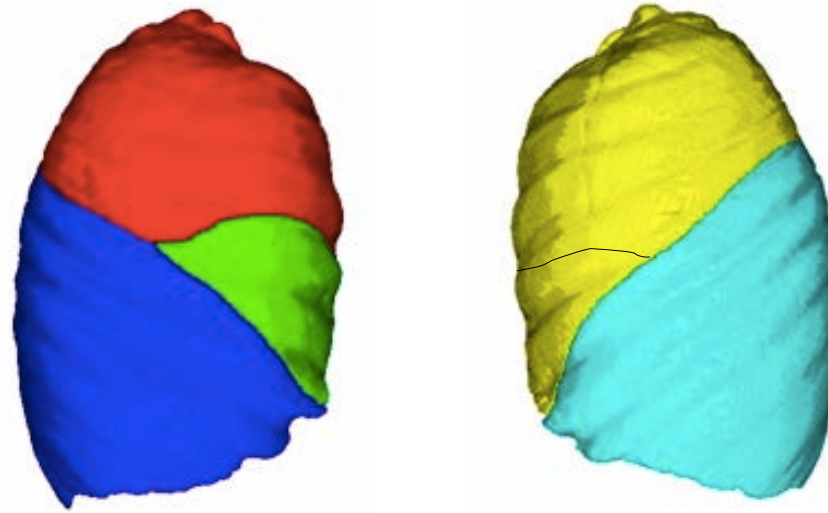


3=51-75%



4=76-100%

Qualitative Emphysema Scoring



$$\text{Total Emphysema Score} = N_{RUL} + N_{RML} + N_{RLL} + N_{LUL} + N_{Lingula} + N_{LLL}$$

Emphysema Progression

Defined as an increase in total emphysema score over the study period

Emphysema Distribution



Paraseptal



Centrilobular

Emphysema Distribution



Centrilobular and Paraseptal

Baseline Characteristics (n=345)

Variable	Median (IQR) or n (%)
Age	49 (45, 53)
Male Sex (%)	311 (90%)
BMI	23.8 (21.9, 26.0)
Current CD4	577 (430, 746)
Nadir CD4	188 (65, 290)
Viral Load <40	267 (77%)
Smoking Status	
Never	64 (19%)
Former	101 (29%)
Current, <10 cig/day	70 (20%)
Current, ≥10 cig/day	96 (28%)
N/A	14 (4%)
Smoking Pack-Years	17 (5, 28)

Baseline Respiratory Characteristics

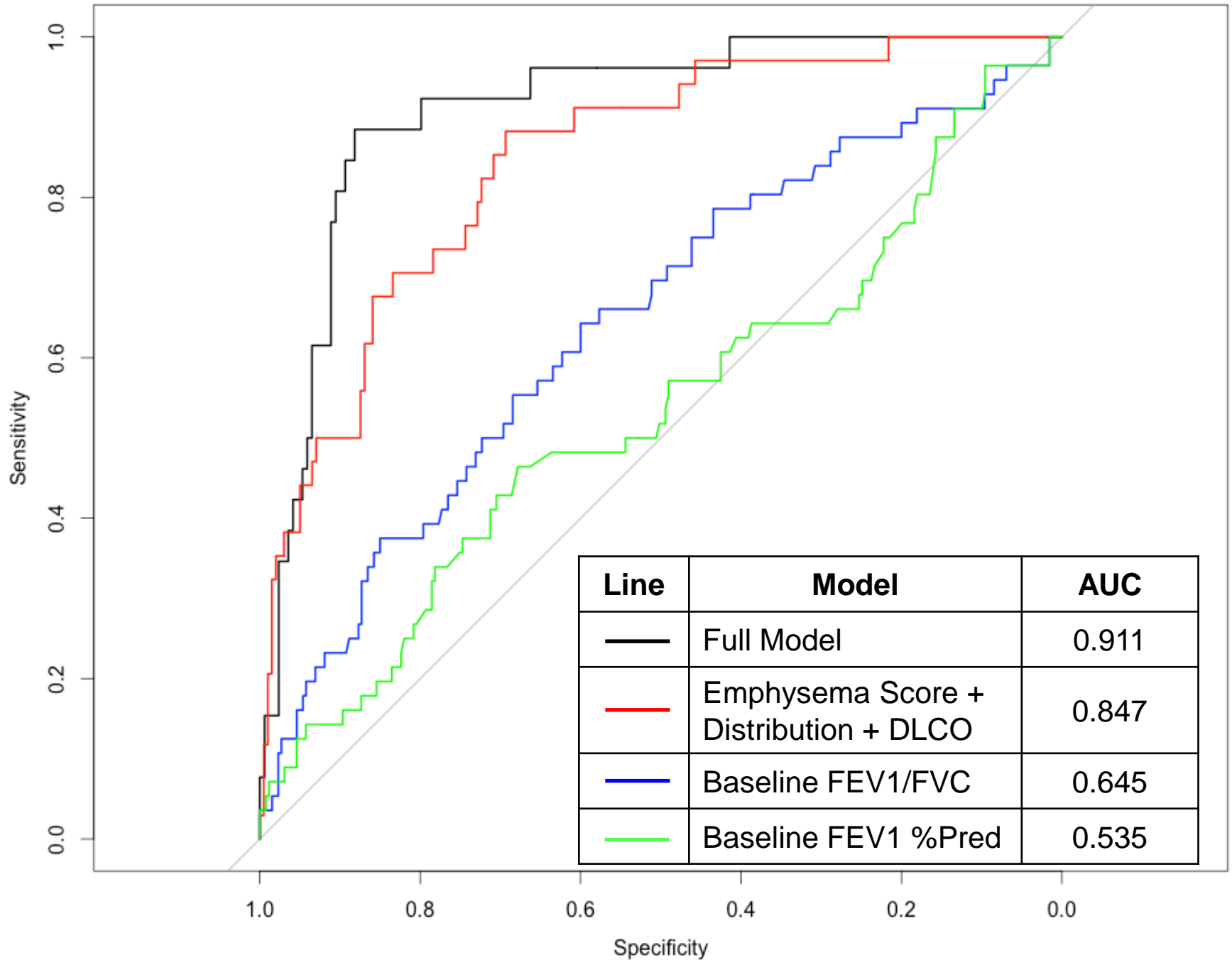
Variable	Median (IQR)
FEV1/FVC	79.3 (75.6, 83.0)
FEV1 (% Pred)	106.1 (96.7, 116.8)
FVC (% Pred)	109.0 (98.3, 118.0)
TLC (% Pred)	114.6 (106.1, 122.9)
DLCO (% Pred)	75.2 (65.7, 87.2)
Baseline Emphysema Score	0 (0, 3)

Variable	Progressor (n=60)	Non-Progressor (n=285)	P-value
Emphysema Score	4 (1, 6)	0 (0, 2)	7.81e-14
Emphysema Type			
Centrilobular	3 (5%)	40 (14%)	1.13e-13
Paraseptal	9 (15%)	34 (12%)	
Combination	37 (62%)	41 (14%)	
Smoking Status			
Never or Former	15 (25%)	150 (53%)	8.89e-06
<10 cigs/day	11 (18%)	59 (21%)	
≥10 cigs/day	32 (53%)	64 (22%)	
NA	2 (3%)	12 (4%)	
Smoking Pack-Years	22.5 (15.3, 31.8)	15.0 (1.0, 26.0)	0.0001
DLCO (%Pred)	64.75 (54.27, 78.08)	77.50 (68.15, 88.00)	0.0004
FEV1/FVC (%)	77.05 (72.44, 80.39)	79.78 (76.42, 83.55)	0.0007
BMI	22.93 (20.73, 24.61)	23.96 (21.98, 26.21)	0.0107
Male Sex	59 (98%)	252 (88%)	0.0159
Albumin	4.6 (4.3, 4.8)	4.7 (4.5, 4.9)	0.0379

Multivariable Logistic Regression Model

Outcome Variable: Emphysema Progression

Parameter	Estimate	Std. Error	P-value
(Intercept)	0.740	0.308	0.017
Baseline DLCO (% Pred)	-0.004	0.002	0.0005
Centrilobular and Paraseptal Distribution	0.241	0.097	0.013
Male Sex	0.100	0.078	0.200
Total Exposure to Integrase Inhibitors (Months)	-0.002	0.002	0.255
BMI	-0.007	0.007	0.277
Baseline Emphysema Score	0.017	0.018	0.332
Albumin	-0.335	0.349	0.338
Current Smoker ≥ 10 cigarettes/day	-0.054	0.072	0.453
Duration of HIV (Months)	-0.0002	0.0003	0.560
ASCVD (Cardiovascular Risk Score)	0.002	0.004	0.661



Comparisons to Non-HIV Population

- **Non-HIV Study Population**
 - 1,295 HIV- patients with ≥ 2 chest CT scans
 - Enrolled in the Pan-Canadian Early Detection of Lung Cancer Study
- **Qualitative Emphysema Scoring**
 - Total emphysema score
 - 1 = <5% (Trivial)
 - 2 = 5-25% (Mild)
 - 3 = 26-50% (Moderate)
 - 4 = 51-75% (Severe)
 - 5 = 76-100% (Very Severe)

Matched Cohorts

Variable	HIV (n=301)	Non-HIV (n=301)	P-value
Age (years)	49 (45, 54)	63 (60, 67)	2.2e-16
Male Sex	271 (90%)	271 (90%)	1
BMI (kg/m ²)	23.9 (21.9, 26.1)	25.4 (23.5, 27.9)	1.269e-09
Smoking Status			
Current	142 (47%)	202 (67%)	2.2e-16
Former	97 (32%)	99 (33%)	
Never	62 (21%)	0 (0%)	
Smoking Pack-Years	17.0 (4.3, 26.0)	50.0 (41.3, 61.3)	2.2e-16
Maximum Time Interval (years)	3.01 (2.03, 4.24)	3.01 (2.03, 4.23)	0.9865
Emphysema Progressor	46 (15%)	52 (17%)	0.5809

Limitations

- Slight differences in emphysema scoring technique may limit comparisons to the non-HIV population.
- What is the appropriate HIV-negative control population?
- The practicalities of prediction model validation

Conclusions

- Emphysema progression in HIV can be predicted by baseline severity, distribution, and diffusion capacity
- These may be useful tools for the HIV clinician to identify high-risk patients in need of aggressive smoking cessation programs and COPD treatments
- Even younger HIV-infected patients with lesser smoking habits exhibit a similar prevalence of emphysema progression compared to HIV-uninfected patients

Future Directions

- Validation of predictive model in additional HIV cohorts with available CT imaging
- Determining the impact of emphysema progression on morbidity and mortality in HIV
- Identifying additional blood or lung-based biomarkers for emphysema progression in HIV
- Using next generation sequencing in lung tissue to identify the molecular determinants of emphysema progression in HIV

Thank You

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